Armed Forces College of Medicine

AFCM

Case study

Medical Microbiology &

Immunology department

Case

A 27-year-old male manual worker developed headache on September 8 that worsened over the next 2 days. On September 9, he was admitted to the hospital with severe headache, temperature of 39.5°C, chills, and vomiting. He had a lumbar puncture with no recorded opening pressure, 20 red blood cells, 0 white blood cells, a protein level of 680 g/L, and a normal glucose level. Treatment was started with antibacterial agents and he was transferred to ICU, on September 11 because of deteriorating mental status. Another lumbar puncture showed an opening pressure of 280 mm of water, clear fluid, 6 white blood cells (differential cell count: lymphocytes, 0.84), protein level of 1240 g/L, and a

The treating physicians felt a non-focal neurologic examination would be useful, but he was very agitated and combative and was sedated and intubated. The remainder of his examination was notable for a temperature of 40.3° C and acyclovir therapy was added to broad-spectrum antibacterial agents. Detailed neurologic examination was not possible but the neurology consultant noted that the patient had minimally responsive pupils both directly and consensually and an absent corneal reflex on the left side. He had spontaneous movements of all 4 extremities and withdrew from painful tactile stimuli. He also had multifocal myoclonus. Reflexes and flexor plantar

Case

Magnetic resonance imaging (MRI) of the brain was performed on September 12 and showed an abnormally high signal on T2-weighted images in the pontinetegmentum and area postrema of the medulla, with only minimal postgadolinium enhancement in these area. At this time, these findings were thought to be nonspecific and consistent with encephalitis, vasculitis, or a demyelinating process. On September 13, the serum creatine kinase level was elevated and an electroencephalogram showed diffuse slowing with no abnormal spike activity.

Case

On September 14, the patient's fever dropped and he was somewhat more alert at times and occasionally responsive to commands, but significant agitation necessitated continued sedation. On September 15, he was noted to have persistent upward gaze deviation, absent oculocephalic reflexes, and absent corneal reflexes bilaterally, and was completely unresponsive to verbal or tactile stimuli. His pupils were small but minimally reactive. His stretch and plantar reflexes were unchanged. An electroencephalogram, repeated to rule out status epilepticus as the cause of tonic eye deviation, showed .diffuse slowing with no epileptiform activity

Case

On September 18, the patient was noted to have no remaining brainstem function. The invasiveness of his level of care was diminished, and he died on September 21.

The diagnosis of rabies was first considered on September 12 because the patient had a history of multiple exposures to animals. A cerebrospinal fluid sample from September 12 and serum sample from September 13 were sent for rabies testing; both results were positive.

Q1 :What is the pathogenesis of rabies virus?

Answer

A-Animal reservoirs

- Dogs & cats
- Wild carnivores e.g. foxes and wolves
- Bats

B-Modes of transmission

1-The bite or scratch by a rabid animal

Rabies virus is present in saliva of rabid animal e.g Dogs (main source)

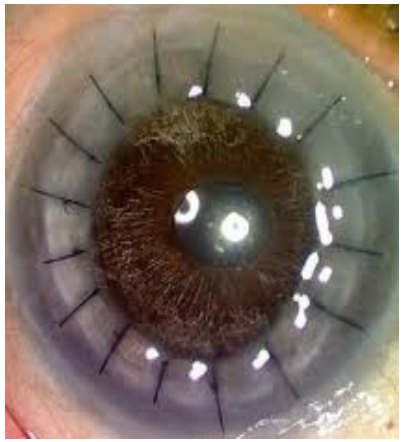
Manifest aggressive, biting behavior induced by the viral encephalitis

2-Non-bite exposures

1-Exposure to aerosols of bat secretions (healthy)& in laboratory works

2- Corneal transplantation (very rare) : from infected humans who died from


Brain inflammation
Virus transmitted by infected saliva through bite or wound
ADAM.



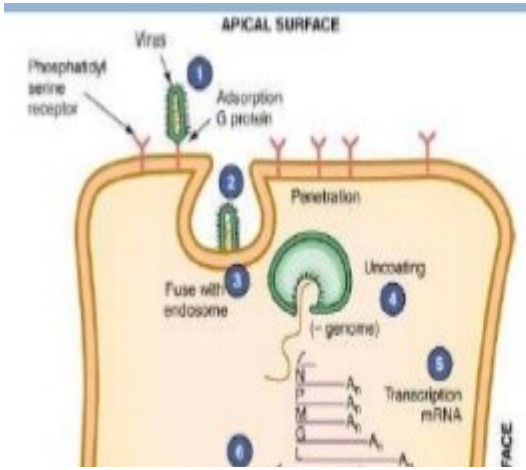
C- Site of replication

The virus replicates in striated muscles at the site of bite → Infects the sensory neurons by attaching to acetylcholine receptors→ Retrograde axonal transport → Move along the peripheral nerves to the spinal cord & brain → Multiplication

D-Effect on nerve cells

- **Encephalitis**
- **Demyelination → Neuronal death**

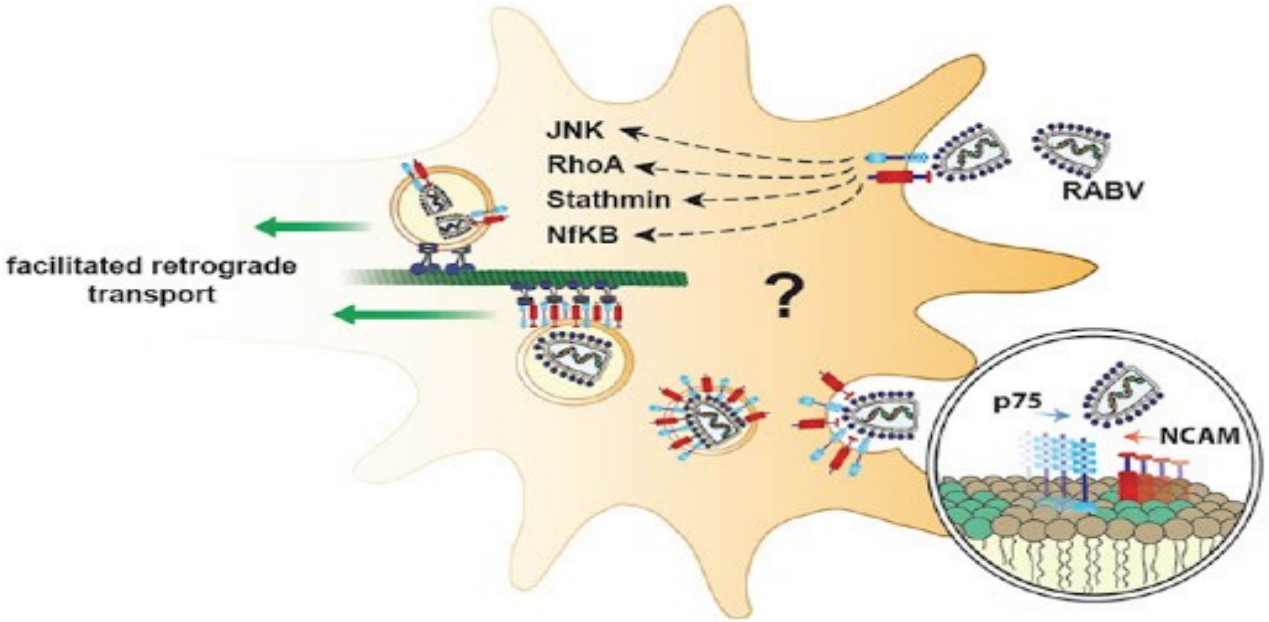
Negri bodies→ Intracytoplasmic inclusion● in nerve cells



BINDS WITH Ach-Choline receptor

Endosomal fusion and uncoating

RNA-RNA pol transcribe mRNA



E - Viral spread

1-Virus migrates via peripheral nerves to :

a-Salivary glands → saliva → transmitted by bite

b-Eye , skin & Kidneys

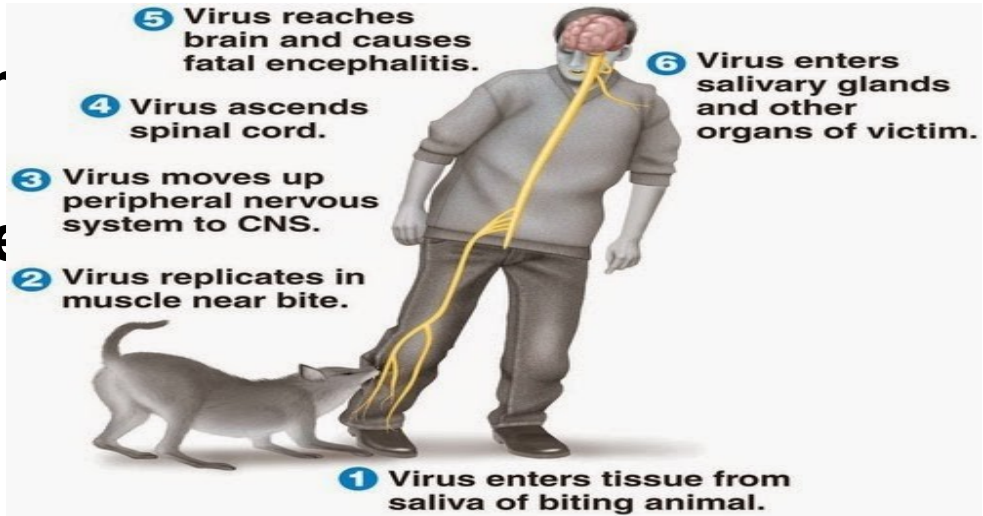
2- Viral replication is restricted to neuronal tissues ⬇

with no viremia

⬇

Virus is protected fror

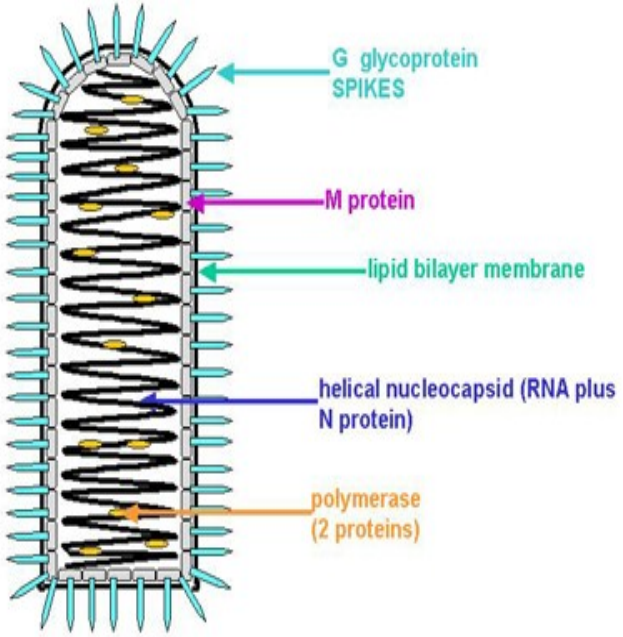
No or little immune re



Q2: What is the structure of rabies virus?

Answer

A-Family : Rhabdovirus



B-Nucleocapsid :

1-ssRNA

2-Helical

3- Bullet shaped

C-Enveloped with glycoprotein projections :

a-Antigen (single antigenic type.)

b-Viral attachment → Target of neutralizing Abs

Q3: What is the clinical presentation of rabies virus?

Symptoms:

- **Fever**
- **Impaired consciousness**
- **Epileptic seizures**
- **Headache**
- **Neck stiffness**

Q4: How to suspect rabies in patient with encephalitis?

Answer

1.History of exposure to animals
2. Laboratory tests

Q5:What are the preventive measures that could prevent the development of rabies ?

Answer

Post exposure management of a human bitten by an animal:

A) Prompt and adequate treatment of all skin wounds possibly contaminated with rabies virus (animal bites and scratches).

1. Thorough cleansing with soap solution or a detergent and flushing of the wound with water. Then apply 70% ethanol or povidone iodine.

2. The wound should not be sutured immediately.

3. The use of antibiotics and tetanus prophylaxis may be indicated.

B) Post-exposure immunization

Vaccines:

1. **Human diploid cell vaccine (HDCV):** It gives rapid, high and greater conversion of antibody titer. It has less serious reactions and less common side effects such as headache, nausea, vomiting, abdominal pain, muscle pain and dizziness.
2. **Rabies vaccine adsorbed (RVA):** Is used since the 1980s.

Answer

● **Both vaccine regimens:** **5 doses for those not previously vaccinated (each 1 ml)**

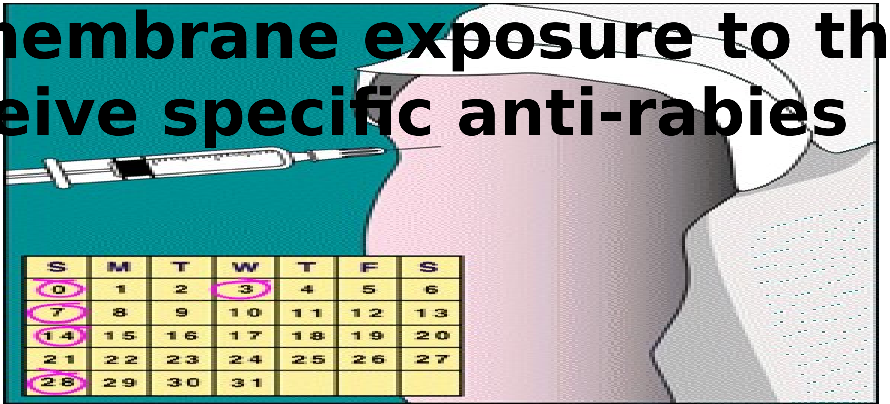
● **The first dose: is given as soon as possible after the bite (day 0) then on days 3, 7, 14 and 28 of the first dose.**

Intramuscular in deltoid region or in the anterolateral upper thigh. It is never given in the gluteal region.

● **For previously vaccinated: Give 2 doses; on days 0 and 3.**

● **Pregnancy and infancy:** **Are never contraindications to post-exposure rabies vaccination**

● **Immunization of contacts:** **Contacts who have an open wound or mucous membrane exposure to the patient's saliva must receive specific anti-rabies treatment.**



C) Rabies immune globulin "RIG": (Passive immunization)

1. It is of human origin.
2. Should be given to all humans bitten by animals whose rabies could not be excluded. e.g. (the animal escaped). However, it is not indicated to those who received pre-exposure vaccine.
3. Half the dose is given through infiltration of the wound and the other half given IM to elicit active immunity.
4. It neutralizes the virus in the bl